SECTION 6: KIDNEY CARE

Concern	Care/Test	Frequency
Kidney Care	♦ Check albumin/creatinine ratio using a random urine sample, also called urine microalbumin/creatinine ratio (**see Algorithm 2**)	*Type 1*: Begin with puberty or after 5 years duration, then annually *Type 2*: At diagnosis, then annually
	♦ Check serum creatinine	At diagnosis, then annually
	♦ Perform routine urinalysis	At diagnosis, then as indicated

Diabetes is the leading cause of kidney failure in the United States. If aggressive intervention is not initiated, individuals with diabetic kidney disease usually progress to kidney failure within five to seven years. Progression of diabetic kidney disease is influenced primarily by glycemic control and blood pressure. Early detection and intervention, along with improved glycemic and blood pressure control, can help reduce the risk of the development and progression of nephropathy. Screening for, and treatment of, diabetic kidney disease adds years to life and is proven to be cost-effective.

Screening for Kidney Disease and Interpreting the Results

Kidney disease in people with diabetes progresses from microalbuminuria (loss of small amounts of albumin) to macroalbuminuria (loss of large amounts of albumin), and eventually leads to loss of kidney function. People with Type 2 diabetes should be screened for microalbuminuria at the time of diagnosis and annually thereafter. People with Type 1 diabetes should be screened at five years of disease duration or at the onset of puberty (whichever occurs first), and annually thereafter. More frequent screening may be indicated for certain groups, such as those with a family history of kidney disease and/or hypertension, those with a history of chronically poor glycemic control, and those of African American, Hispanic/Latino, or American Indian heritage.

A random urine sample measuring the albumin/creatinine ratio, sometimes called the urine microalbumin/creatinine ratio, is recommended as the most accurate and easiest test. Check with your lab to find out how you will need to order the albumin/creatinine ratio, as a lab may request that you order a urine microalbumin and a urine creatinine together (see Table 10). While some labs will provide the calculated ratio, others may not, making it necessary to calculate the ratio yourself. There are several other ways to measure urine microalbumin; however, these tend to be less accurate or in timed collections, such as overnight or 24-hour urine collections, more cumbersome and fraught with collection error.

Albumin excretion can vary from day to day and can be affected by uncontrolled blood pressure, high blood glucose, fever, urinary tract infection, and strenuous physical activity. It is therefore recommended that an elevated value be confirmed over approximately 3 – 6 months before microalbuminuria is diagnosed.

A routine urinalysis/dipstick for protein is not sensitive enough to detect microalbuminuria and is therefore not an appropriate test for early detection of diabetic kidney disease.

Example: Calculating the albumin/creatinine ratio in mg/g

If the urine microalbumin is 10 mg/L and the urine creatinine is 100 mg/dL, then the albumin/creatinine ratio is 10 mg/g. In this example, you first need to multiply the urine creatinine value by 10 in order to convert mg/dL to mg/L (i.e., 100 mg/dL x 10 dL/L = 1000 mg/L). Then simply divide the urine albumin value (10 mg/L) by the urine creatinine value (1000 mg/L) to arrive at the ratio (10 mg/L / 1000 mg/L = 0.01). Then multiply by 1000 to express the value as (mg albumin/g creatinine). If the two values are already in the same units, simply divide the albumin value by the creatinine value and then multiply by 1000.

Once a person has an albumin/creatinine ratio of >300 mg/g (macroalbuminuria), urine protein excretion can be followed using the protein/creatinine ratio. The protein/creatinine ratio is measured from a random urine sample and can be used to follow progression of kidney disease and response to therapy.

Table 10: Albumin/Creatinine Ratio Results

Condition	Value
Normal	< 30 mg/g
Microalbuminuria	30-300 mg/g
Macroalbuminuria	> 300 mg/g

A routine urinalysis should be obtained when a person is diagnosed with diabetes and then checked as indicated to assess for infection, ketones, or any other abnormalities.

Further Evaluation of Kidney Disease

Once persistent microalbuminuria or macroalbuminuria has been detected, a full evaluation of kidney disease should be completed. The estimated Glomerular Filtration Rate (GFR), derived from a serum creatinine, is the best marker of kidney function. Prediction equations estimate GFR based on a serum creatinine and other individual characteristics. Multiple equations exist that can be used to estimate GFR. The Cockcroft Gault equation is useful but requires a person's weight. The Modification of Diet in Renal Disease (MDRD) Study equation uses only serum creatinine, age, gender, and race. While the MDRD Study equation requires a calculator with exponential functions, multiple online resources provide a calculator that estimates GFR:

1) http://www.nkdep.nih.gov/GFR-cal-adult.htm
2) http://www.kidney.org/kls/professionals/gfr_calculator.cfm

The MDRD Study equation is most accurate for individuals with estimated GFRs < 60 ml/min/1.73 m^2 (stage 3 chronic kidney disease and higher). Individuals with diabetic kidney disease should be staged according to the level of estimated GFR (see Table 11). Based on the level of estimated GFR, individuals with diabetic kidney disease can be placed into one of five stages. This is helpful in designing a clinical action plan.

Table 11: Stages of Chronic Kidney Disease – A Clinical Action Plan

Chronic Kidney Disease Stage	GFR (ml/min/1.73m^2)	Action (including action from preceding stages)
Stage 1: Kidney damage[1] with normal or ↑ GFR	≥ 90	Diagnosis, treatment, treatment of comorbid conditions, slowing progression, cardiovascular disease risk reduction
Stage 2: Kidney damage with mild ↓ GFR	60-89	Estimate progression
Stage 3: Moderate ↓ GFR	30-59	Evaluating and treating complications; consider referral to a nephrologist (preferred)
Stage 4: Severe ↓ GFR	15-29	Preparation for kidney replacement therapy; referral to a nephrologist (if not already done); consider referral for transplantation
Stage 5: Kidney failure	< 15 (or dialysis)	Kidney replacement therapy (if uremia present)

[1] most commonly microalbuminuria

Serum creatinine alone should not be used to estimate kidney function. Measuring creatinine clearance from a 24-hour urine collection does not provide a more precise measure of GFR than that obtained by a prediction equation.

Management of Kidney Disease

Angiotensin-coverting Enzyme (ACE) inhibitors or Angiotensin Receptor Blockers (ARBs) are effective treatments for microalbuminuria or macroalbuminuria, as they slow progression of diabetic kidney disease independent of their effect on lowering blood pressure. The effect of ACE inhibitors/ARB therapy on albuminuria is dose-dependent, with medium to high ACE inhibitor/ARB dose amounts proven effective in clinical trials. Adverse effects from the use of ACE inhibitors and ARBs are more common in people with chronic kidney disease. The most common side effects—early decrease in GFR, hypotension, and hyperkalemia—can usually be managed without discontinuation of the agent. With careful monitoring of therapy, most people, even those with low levels of GFR, can be treated with ACE inhibitors or ARBs.

In addition to ACE inhibitor/ARB therapy, aggressive blood pressure control is a priority. According to recent studies, most people will require more than one antihypertensive agent to obtain the blood pressure target of < 130/80 mmHg. If blood pressure is not at target (< 130/80 mmHg), other agents may be added to the ACE inhibitors/ARBs to achieve blood pressure control (e.g., diuretics, beta-blockers, calcium channel blockers, or sympathetic antagonists). Diuretics may be particularly effective when added to ACE inhibitors or ARBs. For additional information, see the K/DOQI Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease: http://www.kidney.org/professionals/kdoqi/guidelines.cfm.

***Caution*:** ACE inhibitor/ARB therapy should not be prescribed to women of childbearing age not using contraception or to pregnant women.

Periodic Re-evaluation and Monitoring of Therapy

Individuals with diabetes should be re-evaluated annually for kidney disease. This includes checking the albumin/creatinine ratio, blood pressure, and serum creatinine (in order to estimate the GFR). For people with documented kidney disease, intervals for follow-up should be based

on clinical circumstance (i.e., blood pressure, kidney function, potassium level, and medication dose changes). The albumin/creatinine ratio or the protein/creatinine ratio should be repeated every three months to monitor progression of kidney disease and response to therapy.

Referral to a Nephrologist and Coordination of Care

Referral to a nephrologist is recommended in all of the following circumstances:

- The primary care provider feels he or she needs assistance in carrying out the recommended action plan (see Table 11).
- The estimated GFR is less than 30 ml/min/1.73 m^2.
- Loss of kidney function is rapid (i.e., greater than 10-15 ml/min/1.73 m^2 loss per year).
- The blood pressure target cannot be achieved.

Caring for people with kidney disease is challenging and requires expertise from a variety of specialists (e.g., dietitians, mental health care providers, nurses, pharmacists, social workers, etc.), all of whom must carefully integrate diabetes and kidney disease care. Early intervention and timely referrals for consultation with kidney experts and other specialty services can lead to optimal management of diabetes and kidney disease.

Essential Patient Education for Kidney Disease

People with diabetes need to understand their personal risk of kidney disease. Education can be a powerful tool for sharing prevention strategies that help stabilize and/or slow progression of disease. People may benefit from information on recent studies showing the advantages of early screening and treatment options. Screening tests should be explained, and easy-to-understand interpretation of results provided. Educational strategies should take into consideration literacy level/skill and special educational or cultural needs, while respecting the individual's willingness to change behavior. Education may include, but is not limited to, the following:

- Glycemic control is essential to prevent or slow progression of diabetic kidney disease.
- Annual kidney function testing and appropriate follow-up are necessary.
- People in early stages of decreased kidney function are typically asymptomatic.
- Hypertension plays a major role in kidney disease and should be treated aggressively. Multiple medications are common for most people.
- Lifestyle modifications (e.g., weight loss, physical activity, decreased salt, smoking cessation, adequate but not excessive protein) are important in delaying or slowing the progression of kidney disease.
- Adherence to the overall management plan is necessary to avoid complications.
- The importance of kidney function tests.
- Benefits of early referral to a nephrologist for declining estimated GFR and what to expect from the visit.
- Ongoing support and continued reinforcement are essential for self-management and learning to cope with chronic complications of declining kidney function.

Helpful Tool Included in This Section

- Algorithm 2 – Screening and Initial Recommendations for Diabetic Kidney Disease (Microalbuminuria and Macroalbuminuria)

References

1) Molitch ME, DeFronzo RA, Franz MJ, et al. for the American Diabetes Association. Nephropathy in diabetes. *Diabetes Care*. 2004;27:S79-S83.
2) Lewis EJ, Hunsicker LG, Bain RP, Rohde RD of the Collaborative Study Group. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. *NEJM*. 1993;329:1456-1462.
3) Ahmad J, Siddiqui MA, Ahmad H. Effective postponement of diabetic nephropathy with enalapril in normotensive type 2 diabetic patients with microalbuminuria. *Diabetes Care*. 1997;20:1576-1581.
4) Ruggenenti P, Remuzzi G. Nephropathy of type-2 diabetes mellitus. *J Am Soc Nephrol*. 1998;9:2157-2169.
5) Keane WF, Eknoyan G. for the National Kidney Foundation. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): a position paper of the National Kidney Foundation. *Am J Kidney Dis*. 1999;33:1004-1010.
6) UK Prospective Diabetes Study (UKPDS) Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ*. 1998;317:703-713.
7) The Heart Outcomes Prevention Evaluation Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE Study and MICRO-HOPE substudy. *Lancet*. 2000;355:253-259.
8) Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D of the Modification of Diet in Renal Disease Study Group. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Ann Intern Med*. 1999;130:461-470.
9) National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF K/DOQI) Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. Web site located at: http://www.kidney.org/professionals/kdoqi/guidelines.cfm, 2002.
10) Bruno G, Merletti F, Biggeri A, et al. Progression to overt nephropathy in type 2 diabetes: the Casale Monferrato Study. *Diabetes Care*. 2003;26:2150-2155.
11) Holechek M. Glomerular filtration: an overview. *Nephrol Nurs J*. 2003;30:285-292.
12) Bernheim S, Chen S, Gomez M, et al. A better alternative for estimating renal function. *Arch Intern Med*. 2003;163:2248-2249.
13) Swedko PJ, Clark HD, Paramsothy K, Akbari A. Serum creatinine is an inadequate screening test for renal failure in elderly patients. *Arch Intern Med*. 2003;163:356-360.
14) Fox CS, Larson MG, Leip EP, Culleton B, Wilson PW, Levy D. Predictors of new-onset kidney disease in a community-based population. *JAMA*. 2004;291:844-850.
15) Zandbergen AA, Baggen MG, Lamberts SW, Bootsma AH, de Zeeuw D, Ouwendijk RJ. Effect of losartan on microalbuminuria in normotensive patients with type 2 diabetes mellitus. A randomized clinical trial. *Ann Intern Med*. 2003;139:90-96.
16) Levey AS, Coresh J, Balk E, et al. for the National Kidney Foundation. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med.* 2003;139:137-147.
17) Perkins BA, Ficociello LH, Silva KH, Finkelstein DM, Warram JH, Krolewski AS. Regression of microalbuminuria in type 1 diabetes. *N Engl J Med*. 2003;348:2285-2293.
18) Hollenberg NK. Treatment of the patient with diabetes mellitus and risk of nephropathy: what do we know, and what do we need to learn? *Arch Intern Med*. 2004;164:125-130.
19) Bakris GL,Weir MR, Shanifar S, et al. for the RENAAL Study Group. Effects of blood pressure level on progression of diabetic nephropathy: results from the RENAAL study. *Arch Intern Med.* 2003;163:1555-1565.
20) Orlowski J. Update in nephrology. *Ann Intern Med*. 2004;140:106-111.
21) Chen J, Muntner P, Hamm LL, et al. The metabolic syndrome and chronic kidney disease in U.S. adults. *Ann Intern Med*. 2004;140:167-174.

Algorithm 2

SCREENING AND INITIAL RECOMMENDATIONS FOR DIABETIC KIDNEY DISEASE (Microalbuminuria and Macroalbuminuria)